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Dietary intake of fish and n-3 polyunsaturated fatty acids and risks of perinatal depression: The Japan Environment and Children's Study (JECS)

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ABSTRACT

The results of several epidemiological studies and clinical trials investigating the effects of n-3 polyunsaturated fatty acids (PUFAs) on antenatal and postnatal depression remain controversial. We investigated the possible association of dietary intake of fish and n-3 PUFAs with the risks of maternal and paternal psychological distress during pregnancy and of maternal postpartum depression in Japan. From a dataset comprising 104,102 maternal registrations and 52,426 paternal registrations in The Japan Environment and Children's Study, this study analyzed complete data on questionnaires for 75,139, 79,346, and 77,661 women during early pregnancy, mid-late pregnancy, and after pregnancy, respectively, and for 41,506 male partners. Multivariable logistic regression showed reduced risk of psychological distress in the second and third quintiles for fish intake in early pregnancy and in the second to fifth quintile in mid-late pregnancy. No reductions were observed for n-3 PUFA intake in early pregnancy but in the second to fourth quintile in mid-late pregnancy. For postpartum depression, reductions were observed in the second to fourth quintile for fish intake but only in the first quintile for n-3 PUFA intake. As for paternal psychological distress, only the fourth quintile for fish intake showed a significant

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Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; K6, Kessler Psychological Distress Scale; CI, confidence interval; EPA, eicosapentaenoic acid; OR, odds ratio; PUFAs, polyunsaturated fatty acids; DHA, docosahexaenoic acid

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reduced risk but none were shown for n-3 PUFA intake. In conclusion, fish intake was associated with some reduced risk of psychological distress during pregnancy, even for male partners. The associations were weaker for n-3 PUFA intake than for fish intake.

1. Introduction

Recent meta-analyses of observational studies (Grosso et al., 2016) and clinical trials (Mocking et al., 2016; Sarris et al., 2016) revealed that n-3 polyunsaturated fatty acids (PUFAs) might have both preventive and therapeutic effects on depression. The meta-analysis of observational studies showed a significant linear dose-response relationship between fish intake and risk of depression (Grosso et al., 2016). Also, the highest intake level of both total n-3 PUFAs and long-chain n-3 PUFAs (i.e., eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) showed a decreased risk of depression compared with the lowest intake, and dose-response analysis revealed a J-shaped association (Grosso et al., 2016). Of the two later meta-analyses of intervention studies, the first revealed a significant moderate to strong effect in favor of n-3 PUFAs (Sarris et al., 2016) and the other reported a beneficial overall effect of n-3 PUFA supplementation in patients meeting the diagnostic criteria for major depressive disorder (Mocking et al., 2016).

The association of dietary n-3 PUFA consumption and depression is controversial, however, in the case of pregnant women, who are believed to be vulnerable to depression because of decreased n-3 PUFA levels during fetal growth (Rees et al., 2005). Some studies have reported beneficial effects of dietary intake of n-3 PUFAs and/or fish on antenatal and/or postnatal depression (da Rocha and Kac, 2012; Golding et al., 2009; Miyake et al., 2013; Shiraishi et al., 2015), while others have shown no effects (Browne et al., 2006; Miyake et al., 2006; Sontrop et al., 2008; Strom et al., 2009). These mixed and inconclusive findings may be attributable to differences in study design, sample size, duration of follow-up, participant background factors, and/or the tools used to assess depression, suggesting that further research is required. Of the three studies reported from Japan (Miyake et al., 2006, 2013; Shiraishi et al., 2015), the study that prospectively examined the effect of n-3 PUFA intake on the risk of postpartum depression revealed no clear inverse association (Miyake et al., 2006). In the other two cross-sectional studies, while one found an independent association of increased consumption of fish, EPA, and DHA with a lower prevalence of depressive symptoms (Miyake et al., 2013), the other found no beneficial effects of n-3 PUFA intake on these symptoms (Shiraishi et al., 2015).

Most of the relevant research to date has focused on maternal perinatal depression, because until recently it was widely believed that only women are affected by depression during pregnancy. Emerging evidence now indicates that their male partners are also affected by depression in the antenatal and postnatal periods. In Japan, one study showed that 15.1% of male partners showed depressive symptoms during mid-pregnancy and 18.9% during late-pregnancy (Hagino et al., 2006), while another study showed that 6.8% were affected at, on average, 29.9 weeks of pregnancy (Watabe and Asaka, 2016). However, scientific research on the predictors of depressive symptoms in men during pregnancy is still scarce, and as far as we know associations with dietary intake of fish and n-3 PUFAs (α-linolenic acid + EPA + docosapentaenoic acid + DHA) have not been investigated. In this study, we investigated the association in women and their male partners during pregnancy, using data from The Japan Environment and Children's Study (JECS).

2. Methods

2.1. Study population

The methods of JECS have been described in detail elsewhere (Kawamoto et al., 2014; Michikawa et al., in press). Briefly, JECS is a nationwide government-funded birth cohort study that is evaluating the impact of various environmental factors on children's health and development. The pregnant women participating in JECS were recruited from 15 areas in Japan between January 2011 and March 2014 (Kawamoto et al., 2014; Michikawa et al., in press). The present study is based on the jecs-ag-20160424 dataset that was released in June 2016 and the allbirth_revice001_ver001 dataset that was released in October 2016. The full dataset is for 104,102 maternal registrations, 6648 of which we excluded because of multiple registration in the study and/or multiple births (Fig. 1). We also excluded data for 29 pregnancies in women who withdrew from the study and for women who gave incomplete answers on the questionnaires, leaving the following for final analysis: data for 75,139 pregnancies in the first trimester, 79,346 pregnancies in the second or third trimester, and 77,661 pregnancies in the postpartum period. Similarly, 2747 of the 52,426 male partners registered in the dataset were excluded because of multiple entries for different pregnancies and/or multiple births by their partner (in such case data for only one birth was used for analysis), leaving 49,679 subjects. We excluded a further 9 subjects who withdrew and 8164 subjects who gave incomplete answers on the questionnaires. This left data for 41,506 male partners for the final analysis (Fig. 1).

The study protocol was approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the Ethics Committee of the University of Toyama. Written informed consent was obtained from all participating women and their male partners.

2.2. Measurements

See Supplementary Methods for details of the following measurements used: self-administered questionnaires; Kessler Psychological Distress Scale (K6); Edinburgh Postnatal Depression Scale (EPDS); and dietary intake of fish and n-3 PUFAs.

2.3. Statistical analysis

Data are expressed as the means ± SD or median unless stated otherwise. To estimate the risks of psychological distress and postpartum depression for each level of fish intake and n-3 PUFA intake, we categorized the participants according to quintile for fish intake or n-3 PUFA level. We then performed logistic regression analysis to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Tests for trend involved assigning categorical numbers to quintile distributions for fish intake and n-3 PUFA intake and evaluating these as continuous variables. Psychological distress during pregnancy was analyzed with adjustment for age, energy intake, number of previous deliveries, pre-pregnancy BMI, highest educational level, annual household income, marital status, alcohol intake, smoking status, morning sickness, physical activity, history of anxiety disorder, history of depression, and employment status. Presence of neonatal physical anomaly was added for analysis of postpartum depression. For male partners, marital status, morning sickness, and physical activity were excluded from the adjustment and the female partner's psychological distress status was added. The association of change in dietary intake of fish and n-3 PUFAs between periconception and pregnancy with psychological distress was also analyzed. The covariates used in this analysis were the same as those mentioned above except for energy intake (in which the average energy intake of the first trimester and second/third trimester was used). Pearson's correlation coefficient was used to calculate the correlation between maternal and paternal fish intake.

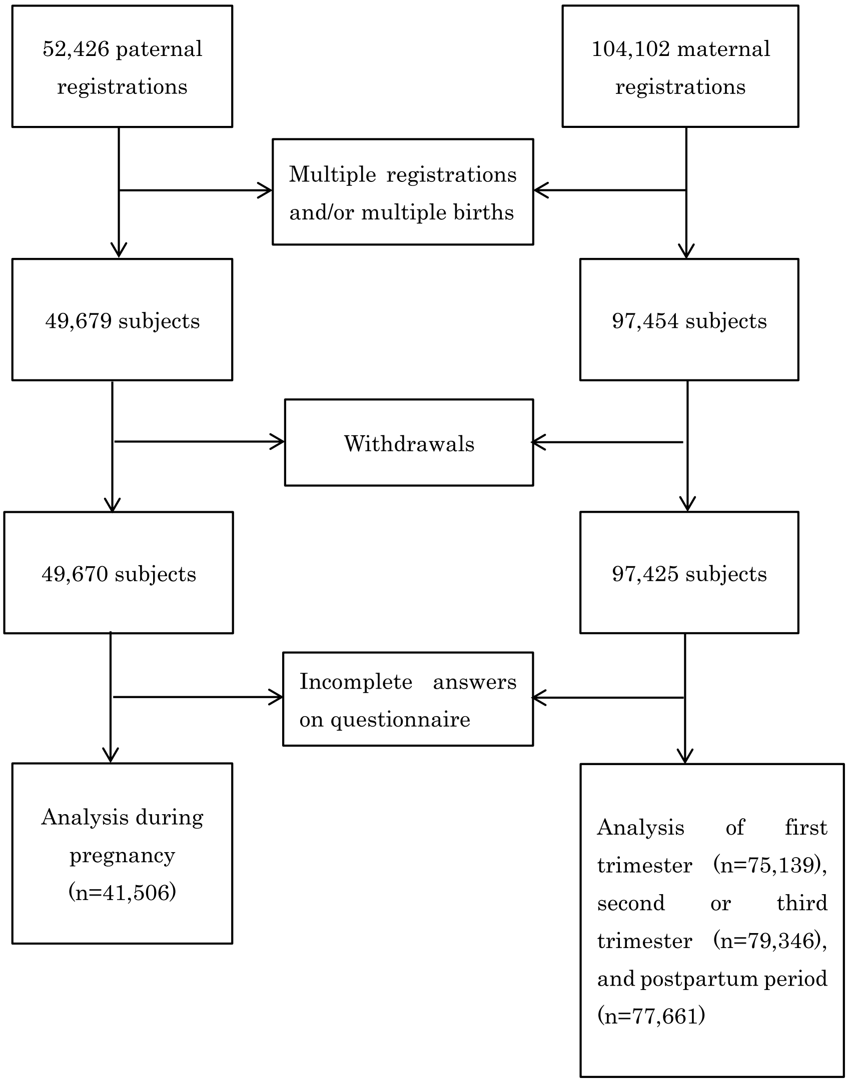

Fig. 1. Flow diagram of the recruitment and exclusion process for pregnant women and their male partners in this study.
The full dataset is for 104,102 maternal registrations, 6,648 of which we excluded because of multiple registration in the study and/or multiple births. We also excluded data for 29 pregnancies in women who withdrew from the study and for women who gave incomplete answers on the questionnaires, leaving the following for final analysis: data for 75,139 pregnancies in the first trimester, 79,346 pregnancies in the second or third trimester, and 77,661 pregnancies in the postpartum period. Similarly, 2747 of the 52,426 male partners registered in the dataset were excluded because of multiple entries for different pregnancies and/or multiple births by their partner (in such case data for only one birth was used for analysis), leaving 49,679 subjects. We excluded a further 9 subjects who withdrew and 8,164 subjects who gave incomplete answers on the questionnaires. This left data for 41,506 male partners for the final analysis.

Two-sided *p* values of less than 0.05 were considered to indicate statistical significance. Data were analyzed using SAS version 9.4 software (SAS Institute Inc., Cary, NC).

3. Results

3.1. Participant characteristics

Maternal characteristics in the first trimester according to quintile for fish consumption are shown in Table 1 and quintile for n-3 PUFA consumption in Supplementary Table 1. Compared with women who reported low fish consumption, those who reported higher fish consumption had a higher energy intake, were slightly older, and were more likely to be multiparous, have a higher level of education and higher annual household income, be a current drinker, be more physically active, and be more likely not to smoke. Very similar associations were observed for dietary n-3 PUFA intake as well as for the second/third trimester in women (Supplementary Tables 2 and 3) and for their male partners during pregnancy (Supplementary Tables 4 and 5). No correlation was found between maternal and paternal fish intake (r = 0.15, n = 37,262).

3.2. Prevalence of psychological distress and postpartum depression

During the follow-up, we documented psychological distress (K6 ≥13) in 3.4% of women in the first trimester (2527/75,139) and 3.1% (2475/79,346) in the second/third trimester. Prevalence of maternal postpartum depression (EPDS ≥9) 1 month after delivery was 13.8% (10,732/77,661). Prevalence of paternal psychological distress (K6 ≥13) during the pregnancy was 1.9% (776/41,506).

3.3. Multivariable logistic regression for maternal psychological distress and maternal postpartum depression

Table 2 shows the multivariable ORs for psychological distress and 95% CIs according to quintile for fish and n-3 PUFA intake during the first trimester (n = 75,139). Multivariable logistic regression of fish intake revealed that ORs for the second and third quintiles were significantly lower (0.83; 95% CI 0.73–0.94 and 0.79; 95% CI 0.70–0.91, respectively). However, no significant associations were observed in this model. Multivariable logistic regression of n-3 PUFA intake showed no association with psychological distress.

Table 3 shows the results of the same analysis as in Table 2 but for a different period (second/third trimester) and with the addition of change in dietary intake between periconception and pregnancy of both fish and n-3 PUFAs. For fish intake, ORs for the second to fifth quintile were significantly lower compared with the reference level, with the lowest OR recorded for the fourth quintile (0.71; 95% CI 0.63–0.82). The trend test also showed a significant inverse association (p = 0.01). As for the change in dietary fish intake, only ORs for the second and

Table 1
Characteristics according to quintile for fish intake in the first trimester of pregnancy in women (n = 75,139).

	Quintile for fish intake				
	1 (low)	2	3	4	5 (high)
Median intake of fish [a], g/day	7.3	20.3	31.5	45.7	75.8
Median intake of calories [a]	1376	1525	1653	1809	2168
Age at baseline questionnaire, years	29.8	30.7	31.2	31.5	31.6
Previous deliveries, n (%)					
Nullipara	7976 (52.9)	6754 (45.2)	6091 (40.7)	5918 (39.0)	5573 (37.2)
Multipara	7102 (47.1)	8188 (54.8)	8870 (59.3)	9243 (61.0)	9424 (62.8)
Pre-pregnancy BMI, kg/m^2 (%)					
< 18.5	2508 (16.6)	2511 (16.8)	2337 (15.6)	2282 (15.1)	2300 (15.3)
18.5- < 25	10,964 (72.7)	11,004 (73.6)	11,100 (74.2)	11,327 (74.7)	10,929 (72.9)
≥25	1606 (10.7)	1427 (9.6)	1524 (10.2)	1552 (10.2)	1768 (11.8)
Highest educational level (%)					
Junior high school or high school	6352 (42.1)	5413 (36.2)	4867 (32.5)	4687 (30.9)	4737 (31.6)
Technical junior college, technical/vocational college or associate degree	6060 (40.2)	6224 (41.7)	6446 (43.1)	6645 (43.8)	6522 (43.5)
Bachelor's degree, postgraduate degree	2666 (17.7)	3305 (22.1)	3648 (24.4)	3829 (25.3)	3738 (24.9)
Annual household income, JPY (%)					
< 4 million	7123 (47.2)	6059 (40.6)	5544 (37.1)	5381 (35.5)	5529 (36.9)
4–6 million	4622 (30.7)	4937 (33.0)	5091 (34.0)	5252 (34.6)	4926 (32.8)
> 6 million	3333 (22.1)	3946 (26.4)	4326 (28.9)	4528 (29.9)	4542 (30.3)
Marital status (%)					
Married (including common law marriage)	14,211 (94.3)	14,341 (95.9)	14,469 (96.7)	14,684 (96.8)	14,509 (96.8)
Single (never married)	699 (4.6)	486 (3.3)	385 (2.6)	378 (2.5)	365 (2.4)
Divorced or widowed	168 (1.1)	115 (0.8)	107 (0.7)	99 (0.7)	123 (0.8)
Alcohol intake (%)					
Never	5464 (36.2)	5211 (34.9)	5113 (34.2)	4996 (33.0)	4868 (32.5)
Ex	8341 (55.4)	8243 (55.1)	8230 (55.0)	8446 (55.7)	8442 (56.3)
Current	1273 (8.4)	1488 (10.0)	1618 (10.8)	1719 (11.3)	1687 (11.2)
Smoking status (%)					
Never	8929 (55.1)	8688 (58.2)	9116 (60.9)	9209 (60.8)	8920 (59.5)
Did previously but quit before learning of pregnancy	3365 (22.3)	3590 (24.0)	3425 (22.9)	3629 (23.9)	3645 (24.3)
Did previously but quit after learning of pregnancy	2495 (16.5)	2001 (13.4)	1836 (12.3)	1743 (11.5)	1753 (11.7)
Currently smoking	923 (6.1)	663 (4.4)	584 (3.9)	580 (3.8)	679 (4.5)
Morning sickness (%)					
Never	2741 (18.2)	2575 (17.2)	2467 (16.5)	2536 (16.7)	2478 (16.5)
Nausea but no vomiting	6453 (42.7)	6581 (44.1)	6580 (44.0)	6572 (43.4)	6181 (41.3)
Vomiting but able to eat	4247 (28.2)	4189 (28.0)	4306 (28.8)	4412 (29.1)	4565 (30.4)
Vomiting and unable to eat	1637 (10.9)	1597 (10.7)	1608 (10.7)	1641 (10.8)	1773 (11.8)
Physical activity, yes (%)	9979 (66.2)	10,430 (69.8)	10,654 (71.2)	11,036 (72.8)	11133 (74.2)
History of anxiety disorder, yes (%)	478 (3.2)	393 (2.6)	387 (2.6)	386 (2.5)	470 (3.1)
History of depression, yes (%)	477 (3.2)	416 (2.8)	426 (2.8)	448 (3.0)	472 (3.1)
Employed, n (%)	10,041 (66.6)	9487 (63.5)	9338 (62.4)	9416 (62.1)	9456 (63.1)

[a] During the year preceding the questionnaire for the first trimester. BMI, body mass index.

fourth quintiles showed a significantly lower level, and the trend test was not significant. As for n-3 PUFA intake, ORs for the second to fourth quintile were significantly low, with a return of the fifth quintile to the reference level. For the change in dietary n-3 PUFA intake, the results were almost the same as those for change in dietary fish intake.

Table 4 shows the results for maternal postpartum depression. ORs from the second to fourth quintile for fish intake were significantly low, with a return of the fifth quintile to the reference level, and the change

Table 2
Odds ratios (95% confidence intervals) for maternal psychological distress in early pregnancy according to quintile for fish or n-3 PUFA intake during the previous year (n = 75,139).

	Quintile for fish or n-3 PUFA intake					*P*-value for trend
	1 (low)	2	3	4	5 (high)	
Fish intake [a]						
Median intake of fish, g/day	7.3	20.3	31.5	45.7	75.8	
Cases[b], n	593	441	415	496	582	
Adjusted odds ratio[c]	1.00	**0.83 (0.73–0.94)**	**0.79 (0.70–0.91)**	0.95 (0.83–1.07)	0.99 (0.87–1.13)	0.55
n-3 PUFA intake [d]						
Median intake of n-3 PUFAs, g/day	0.91	1.37	1.75	2.20	3.12	
Cases[b], n	510	436	452	501	628	
Adjusted odds ratio[c]	1.00	0.92 (0.80–1.05)	0.95 (0.83–1.09)	1.04 (0.91–1.19)	1.09 (0.94–1.26)	0.09

Bold indicates significance ($p < 0.05$).
[a] Intake of fish during the periconception period (in the previous year).
[b] Psychological distress was defined as a Kessler Psychological Distress Scale (K6) score ≥13.
[c] Covariates were adjusted for age, energy intake, number of previous deliveries, pre-pregnancy BMI, highest educational level, annual household income, marital status, alcohol intake, smoking status, morning sickness, physical activity, history of anxiety disorder, history of depression, and employment status.
[d] Intake of n-3 PUFAs during the periconception period (in the previous year).

Table 3
Odds ratios (95% confidence intervals) for maternal psychological distress in mid-late pregnancy according to quintile for fish or n-3 PUFA intake during pregnancy and quintile for change in intake (n = 79,346).

	Quintile for fish or n-3 PUFA intake					*P*-value for trend
	1 (low)	2	3	4	5 (high)	
Fish intake[a]						
Median intake of fish, g/day	4.7	16.7	27.3	40.7	67.5	
Cases[b], n	643	452	451	394	535	
Adjusted odds ratio[c]	1.00	**0.75 (0.66–0.85)**	**0.78 (0.69–0.89)**	**0.71 (0.63–0.82)**	**0.87 (0.76–0.99)**	**0.01**
Change in fish intake[d]						
Median change, g/day	−34.3	−13.3	−3.2	5.0	22.6	
Cases[b], n	576	438	506	447	508	
Adjusted odds ratio[c]	1.00	**0.83 (0.73–0.95)**	0.96 (0.84–1.08)	**0.87 (0.76–0.99)**	0.90 (0.79–1.02)	0.19
n-3 PUFA intake[e]						
Median intake of n-3 PUFAs, g/day	0.81	1.25	1.61	2.04	2.88	
Cases[b], n	558	455	432	437	593	
Adjusted odds ratio[c]	1.00	**0.87 (0.76–0.99)**	**0.85 (0.75–0.98)**	**0.85 (0.74–0.98)**	1.04 (0.90–1.20)	0.85
Change in n-3 PUFA intake[f]						
Median change, g/day	−1.06	−0.44	−0.12	0.17	0.70	
Cases[b], n	616	440	470	410	539	
Adjusted odds ratio[c]	1.00	**0.84 (0.74–0.96)**	0.90 (0.79–1.02)	**0.78 (0.68–0.88)**	0.92 (0.81–1.04)	0.07

Bold indicates significance ($p < 0.05$).
[a] Intake of fish during pregnancy (after learning of pregnancy).
[b] Psychological distress was defined as Kessler Psychological Distress Scale (K6) ≥13.
[c] Covariates were adjusted for age, energy intake, number of previous deliveries, pre-pregnancy BMI, highest level of education, annual household income, marital status, alcohol intake, smoking status, morning sickness, physical activity, history of anxiety disorder, history of depression and employment status.
[d] Change was defined as the difference in fish intake between periconception and during pregnancy.
[e] Intake of n-3 PUFAs during pregnancy (after learning of pregnancy).
[f] Change was defined as the difference in n-3 PUFA intake between periconception and during pregnancy.

Table 4
Odds ratios (95% confidence intervals) for maternal postpartum depression according to quintile for fish or n-3 PUFA intake during pregnancy and quintile for change in intake (n = 77,661).

	Quintile for fish or n-3 PUFA intake					*P*-value for trend
	1 (low)	2	3	4	5 (high)	
Fish intake[a]						
Median intake of fish, g/day	4.7	16.7	27.3	40.5	67.4	
Cases[b], n	2418	2053	2027	2035	2199	
Adjusted odds ratio[c]	1.00	**0.88 (0.82–0.93)**	**0.90 (0.84–0.96)**	**0.91 (0.85–0.97)**	0.94 (0.88–1.01)	0.23
Change in fish intake[d]						
Median change, g/day	−34.3	−13.3	−3.2	5.0	22.6	
Cases[b], n	2327	1981	2050	2124	2250	
Adjusted odds ratio[c]	1.00	**0.89 (0.83–0.95)**	**0.91 (0.85–0.97)**	0.97 (0.91–1.04)	0.99 (0.93–1.06)	0.30
n-3 PUFA intake[e]						
Median intake of n-3 PUFAs, g/day	0.81	1.25	1.61	2.04	2.88	
Cases[b], n	2219	2039	2056	2084	2334	
Adjusted odds ratio[e]	1.00	**0.92 (0.86–0.98)**	0.98 (0.92–1.05)	0.97 (0.91–1.05)	1.02 (0.94–1.11)	0.32
Change in n-3 PUFA intake[f]						
Median change, g/day	−1.06	−0.44	−0.12	0.17	0.70	
Cases[b], n	2381	1967	2056	2069	2259	
Adjusted odds ratio[c]	1.00	**0.90 (0.84–0.96)**	0.94 (0.88–1.00)	0.95 (0.89–1.02)	0.98 (0.92–1.04)	0.89

Bold indicates significance ($p < 0.05$).
[a] Intake of fish during pregnancy (after learning of pregnancy).
[b] Depression was defined as an Edinburgh Postnatal Depression Scale score ≥9.
[c] Covariates were adjusted for age, energy intake, number of previous deliveries, pre-pregnancy BMI, highest level of education, annual household income, marital status, alcohol intake, smoking status, morning sickness, physical activity, history of anxiety disorder, history of depression, employment status, and presence of neonatal physical anomalies (neonatal physical anomalies were newly added in comparison to Tables 3 and 4).
[d] Change was defined as the difference in fish intake between periconception and during pregnancy.
[e] Intake of n-3 PUFA during pregnancy (after learning of pregnancy).
[f] Change was defined as the difference in n-3 PUFA intake between periconception and during pregnancy.

in dietary fish intake showed a weaker association than fish intake did. Both dietary n-3 PUFA intake and the change in such intake had significantly low ORs in the second quintile.

3.4. Multivariable logistic regression for paternal psychological distress

Table 5 shows the ORs and 95% CIs for paternal psychological distress according to quintile for fish and n-3 PUFA intake during pregnancy (n = 41,506). Multivariable logistic regression revealed significantly low ORs in the fourth quintile for fish intake, but the trend test was not significant. No association was found for dietary n-3 PUFA intake.

4. Discussion

Fish intake showed an association with reduced risk of

Table 5
Odds ratios (95% confidence intervals) for paternal psychological distress according to quintile for fish or n-3 PUFA intake during pregnancy (n = 41,506).

	Quintile for fish or n-3 PUFA intake					*P*-value for trend
	1 (low)	2	3	4	5 (high)	
Fish intake [a]						
Median intake of fish, g/day	4.7	20.7	35.6	53.0	90.3	
Cases[b], n	179	146	138	129	184	
Adjusted odds ratio[c]	1.00	0.80 (0.64–1.00)	0.81 (0.64–1.02)	**0.75 (0.59–0.95)**	1.00 (0.80–1.25)	0.82
n-3 PUFA intake [d]						
Median intake of n-3 PUFAs, g/day	0.89	1.40	1.83	2.36	3.50	
Cases[b], n	155	149	138	137	197	
Adjusted odds ratio[c]	1.00	0.98 (0.78–1.24)	0.88 (0.69–1.12)	0.87 (0.68–1.10)	1.17 (0.93–1.49)	0.47

Bold indicates significance (p < 0.05).
[a] Intake of fish during the periconception period (in the previous year).
[b] Psychological distress was defined as a Kessler Psychological Distress Scale (K6) score ≥13.
[c] Covariates were adjusted for age, energy intake, number of previous deliveries, BMI, educational background, family income, alcohol intake, smoking status, history of anxiety disorder, history of depression, employment status and presence of partner's psychological distress.
[d] Intake of n-3 PUFAs during the periconception period (in the previous year).

psychological distress in women during mid-late pregnancy and some degree of association in early pregnancy. No association was observed between n-3 PUFA intake and risk of psychological distress in early pregnancy, but there was some reduced risk of psychological distress in mid-late pregnancy. For postpartum depression, there was no association between n-3 PUFA intake and risk of depression, but some reduced risk was observed for the second to fourth quintile for fish intake. In relation to paternal psychological distress, the fourth quintile for fish intake showed significantly decreased ORs, but no association was observed for n-3 PUFA intake. To our knowledge, this is the first nationwide community-based prospective research in Japan on the association of fish and n-3 PUFA intake with maternal and paternal psychological distress during pregnancy and with maternal postpartum depression.

Although psychological distress and depression are related, the prevalence of psychological distress during pregnancy in the present study (3.4% in the first trimester and 3.1% in the second/third trimester) was considerably lower than that of maternal depression reported in an earlier systematic review (7.4%, 12.8%, and 12.0% in the first, second, and third trimesters, respectively) (Bennett et al., 2004). The difference in prevalence is probably attributable to the higher K6 cut-off score (≥13) used in the present study, which is indicative of more severe mental illness (Sakurai et al., 2011). In fact, the prevalence of maternal depression in our study is similar to the prevalence of 2.7% measured using the same screening tool but in a different population in a community survey conducted in a Japanese city (Sakurai et al., 2011). The prevalence of postpartum depression observed 1 month after delivery in the present study (13.8%) is also consistent with that observed in a previous study (14.0%) using the same screening tool (Miyake et al., 2006).

Although the prevalence of paternal psychological distress in the present study was lower than that of maternal psychological distress (3.4% in the first trimester and 3.1% in the second/third trimester), psychological distress in male partners may affect the mental health of their pregnant partners, thereby having indirect negative effects on their children's behavioral and emotional status (Kvalevaag et al., 2013, 2014; Ramchandani et al., 2008). With this in mind, we tried, in the same study, to determine whether there was an association of fish intake or n-3 PUFA intake with risk of psychological distress in both parents and found stronger associations in women than in men. The reason for the stronger association found in the pregnant women might be depletion of n-3 PUFA levels during pregnancy. A nationwide study in Germany suggested that week of pregnancy and month of lactation were negatively associated with n-3 PUFA levels in erythrocytes (Gellert et al., 2016). This decline in n-3 PUFA levels during the antepartum and postpartum periods might have caused this association more clearly in women than in men. It is reasonable to assume, then, that there would be a stronger association in the second/third trimester than in the first trimester in pregnant women.

Although a meta-analysis of observational studies revealed significantly lower blood n-3 PUFA levels in patients with perinatal depression (Lin et al., 2017), we found stronger associations for dietary fish intake than for dietary n-3 PUFA intake. If dietary n-3 PUFA intake has a true protective effect, we could expect n-3 PUFA intake to be higher than that for fish, but the opposite was the case in our study. There might be two reasons for this. First, some nutrients in fish other than n-3 PUFAs (i.e., vitamins, minerals, and calcium) may have contributed to the reduced risk of psychological distress and/or depression. Fish is a good source of vitamin D, and a cross-sectional study in Japan reported that vitamin D protected against antenatal depression (Miyake et al., 2015a). As for dietary calcium intake, a cross-sectional study in Japan found a protective linear association between overall intake of calcium and yoghurt and depressive symptoms during pregnancy (Miyake et al., 2015b). The other possible reason is that n-3 PUFAs contain 3 major fatty acids (α-linolenic acid, EPA, and DHA) and a previous meta-analysis showed that dietary intake of EPA + DHA has a more beneficial effect than that of total n-3 PUFAs (relative risk 0.76 [95% CI 0.46–0.90] vs 0.82 [0.72–0.94]) (Grosso et al., 2016). Because the dataset used in the present study did not contain data for individual fatty acids, we were not able to evaluate the effects of fatty acids separately. Furthermore, if we had used a diagnostic tool rather than a screening tool, we might have seen a clearer association, given that a previous meta-analysis found larger differences in serum n-3 PUFA levels in studies of major depressive disorder as defined by Diagnostic and Statistical Manual of Mental Disorders criteria than in studies that did not use the criteria (Lin et al., 2010).

Although the mechanism underlying the association between n-3 PUFA levels and depressive symptoms is not fully understood, a review by Su et al. suggests that 4 factors might be involved: neurotransmitters, inflammation, oxidation, and neuroplasticity (Su et al., 2015). For example, n-3 PUFAs and their counterparts, n-6 PUFAs, might be related to depression via pathways for inflammation. The n-6 PUFAs can be precursors for the pro-inflammatory series of eicosanoids, whereas n-3-derived metabolites are precursors for the anti-inflammatory series of eicosanoids (Simopoulos, 2002), and a meta-analysis showed that a high ratio of n-6 to n-3 PUFAs in blood is associated with perinatal depression (Lin et al., 2017).

Intriguingly, almost all of the associations were U-shaped regardless of their statistical significance. This pattern has been observed in previous dosing studies. Peet and Horrobin (2002) conducted a dose-ranging study with EPA at dosages of 1, 2, or 4 g/d for 12 weeks in patients with depression and found that only the dosage of 1 g/d was effective. Later, Mischoulon et al. (2008) conducted a dose-ranging study with DHA for 12 weeks and found that DHA was effective at the lower doses. The same group then conducted another RCT using low dosage of 1 g/d EPA for 8 weeks and found an advantage over placebo that did not reach statistical significance (Mischoulon et al., 2009). They discussed the reason for the efficacy of low-dose n-3 PUFAs as opposed to high-dose n-3 PUFAs from the viewpoint of n-6/n-3 balance. If there is an optimal n-6/n-3 ratio in humans that maintains a balance between proinflammatory and anti-inflammatory forces, its proper equilibration may prevent or reverse a depressed state (Mischoulon et al., 2009). Furthermore, administration of higher n-3 PUFAs doses could result in an “overcorrection” that dampens the antidepressant effect of n-3 PUFAs. Another reason for this phenomenon might be explained by energy intake. In the present study, fish intake showed a strong linear association with energy intake and a weak association with prevalence of overweight (BMI ≥25). A meta-analysis of 5 cohort studies revealed that overweight predicted depression in women (Jung et al., 2017). Although we adjusted for pre-pregnant BMI and energy intake in this study, there might be residual issues related to these two factors.

The main strength of the present study is its large sample size. To the best of our knowledge, this is the largest study investigating the association of dietary intake of fish and n-3 PUFA with risk of maternal psychological distress during pregnancy and postpartum depression. Our study is also the first to investigate psychological distress during pregnancy in male partners. The study was conducted nationwide (at 15 community-based centers) in Japan, so its subjects are representative of pregnant women in the community. Further, the K6 and EPDS used as screening tools for psychological distress and depression in this study are validated and widely used in Japan.

There are also some limitations to this study. First, the FFQ has not been validated for use with pregnant women. The National Health and Nutrition Survey in Japan, 2012 (Japan Ministry of Health) showed that median intake of fish in women aged 20–29 years and 30–39 years is 30.6 g/day and 35.0 g/day, respectively, with corresponding values in men of 37.5 g/day and 50.0 g/day. These results are slightly higher than ours and the discrepancy may be derived from the methods used (food weighing method vs. FFQ). In general, the FFQ is less accurate than the food weighing method, which might have brought some associations towards the null. Second, because of its observational nature, unmeasured residual factors might have confounded the results. For example, fish consumption may serve as a proxy for a healthy lifestyle in general (Schiepers et al., 2010). Third, subtypes of n-3 PUFAs (alpha-linolenic acid, EPA, docosapentaenoic acid, and DHA) were not included in the dataset. Finally, we excluded about 20,000 women and 7000 men with incomplete answers on the questionnaire. Although these exclusions were necessary for the current analysis, we cannot not rule out the possibility that this introduced a degree of selection bias.

As for implications in the clinical setting, evidence of the efficacy of n-3 PUFAs for perinatal depression is scarce. Although a meta-analysis of the association between blood level of n-3 PUFAs and perinatal depression showed that a lower level of n-3 PUFAs might be a risk factor (Lin et al., 2017), it is still premature to recommend n-3 PUFAs supplementation without a meta-analysis of RCTs for pregnant women. On the other hand, fish contains not only n-3 PUFAs but also minerals and vitamins that are important for maternal and infant outcomes (Ramakrishnan et al., 2012). Therefore, consumption of fish should be recommended for pregnant women, as long as the fish recommended are limited to those not containing methylmercury.

In conclusion, fish intake and n-3 PUFA showed some degree of association with reduced risk of psychological distress in women during mid-late pregnancy, but not much association in their male partners during pregnancy. The associations were weaker for n-3 PUFA intake than for fish intake. Further research such as interventional studies are warranted to confirm our findings.

Contributors

K. Hamazaki had full access to all data and takes responsibility for the integrity of the data and accuracy of the data analysis.

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Conflicts of interest

K.H. has received a grant from the Japan Society for the Promotion of Science. All other authors report no conflicts of interest relevant to this article.

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Appendix

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpsychires.2017.11.013.

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